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Drugs & Biologics

Le webzine du cabinet White-Tillet

Friday November 8, 2013 (SW45 2013)

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«Beyond words, the world »

© Adrien Tillet

NEWS

☞ Johnson & Johnson débourse 2,2 milliards de dollars pour éviter un procès

Le groupe pharmaceutique américain était accusé d'avoir versé des pots-de-vin à des pharmaciens. Un accord a été conclu avec le gouvernement américain pour mettre fin aux accusations.

Les accusations concernent « la promotion pour des usages non approuvés comme sûrs et efficaces par l'autorité américaine des médicaments (FDA) et le paiement de pots-de-vin à des pharmaciens » et des médecins pour la vente pour ces indications des médicaments Risperdal, Invega et Natrecor, détaille le communiqué.

« Le comportement incriminé dans cette affaire a mis en péril la santé et la sécurité des patients », fait valoir le ministre américain de la Justice Eric Holder. … (Source : LesEchos)

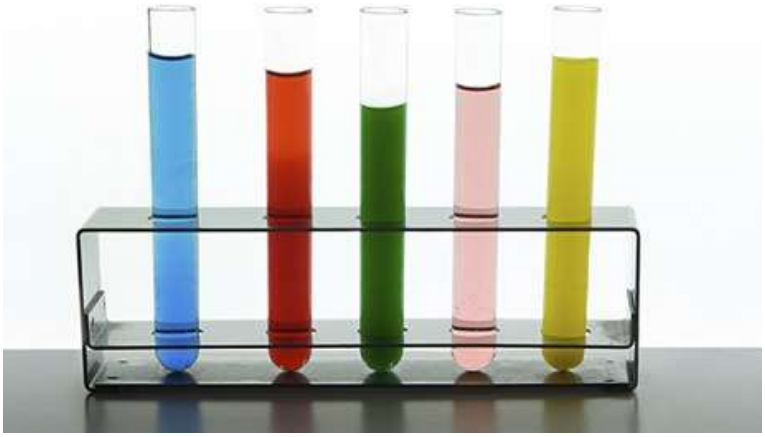
☞ Teva says it may have violated bribery laws around the world

While other countries are scrambling to understand if they have exposure to a Chinese probe into bribery, Teva Pharmaceutical Industries ($TEVA) says it has found it has similar issues elsewhere. The Israeli

drugmaker said in a securities filing that its own investigation has turned up suspect practices in Latin America, Eastern Europe and Russia.

Teva reported in its quarterly report Thursday that it may have violated the U.S. Foreign Corrupt Practices Act (FCPA) and perhaps local laws and could face fines, lawsuits and criminal actions. It said it turned all of the information over to the Securities and Exchange Commission (SEC) and the Department of Justice in the U.S. … (Source: FiercePharma)

☞ Scientists voice fears over ethics of drug trials remaining unpublished



Drug companies and other organisations that carry out clinical trials are violating their ethical obligation to the people who take part by failing to publish the results, scientists will argue on Wednesday.

Almost one in three (29%) large clinical trials in the United States remain unpublished five years after they are finished, according to scientists writing in the British Medical Journal. Of those, 78% have no results at all in the public domain.

The scientists calculate about 250,000 people took part in the unpublished trials and have therefore been exposed to all the risks involved in research without the benefits to society they were led to believe would ensue. This "violates an ethical obligation that investigators have towards study participants", say Christopher Jones from the Department of Emergency Medicine, Cooper Medical School of Rowan University, New Jersey, and colleagues. They call for additional safeguards "to ensure timely public dissemination of trial data." … (Source: TheGuardian)

☞ Merck's Experimental HPV Vaccine Shows Promise in Late-Stage Trial

(Source: WSJ)

☞ AstraZeneca's asthma drug benralizumab advances in Phase III clinical trial

AstraZeneca has started the Phase III Windward program of its biotech drug benralizumab for the treatment of patients with severe asthma.

MedImmune, the company's biologics research and development (R&D) unit, is responsible for developing benralizumab, a monoclonal antibody binding to the interleukin-5 receptor (IL-5Ra) that reduces eosinophils.

Eosinophils are a type of white blood cells which play a major role in the cause and extremity of asthma and its side-effects.

According to the company, in patients with elevated eosinophil counts, treatment with an IL-5 inhibitor in addition to guideline-based strategies might improve their asthma control and decrease the frequency of asthma attacks. … (Source: PBR)

WORLDWIDE

Government and Regulatory Bodies

http://www.pharmweb.net/pwmirror/pwk/pharmwebk.html

http://www.who.int/en/

☞ WorldMedical Association Declaration of Helsinki Ethical Principles for Medical Research Involving Human Subjects (64th WMA General Assembly, Fortaleza, Brazil, October 2013)

World Medical Association Declaration of Helsinki 2013.pdf

☞ Pharma's Transparency Troubles

It seems like open season on the pharmaceutical industry. Academics and consumer activists charge pharma companies with hiding clinical trial information on medical product safety, fueling the campaign to expand public access to confidential research information. The federal government's "Sunshine" program for disclosing financial ties between industry and physicians reflects a lengthy campaign to curb marketing tactics perceived to boost inappropriate prescribing. Media reports regularly attack high drug prices, both for life-saving specialty drugs and for widely used treatments such as asthma inhalers. And recent disclosures raise questions about too-close ties between pharma companies and Food and Drug Administration officials. … (Source: PharmExec)

☞ Biotech research requires strong protections

Recent biopharmaceutical advancements are changing the way we think about medicine. "Biologics" are being manufactured from living cells to treat sickness at the most basic biological level. These drugs are far more complex and effective than traditional chemical-based medicines.

Texas-based research centers are testing, for example, a virus-based biologic that may someday treat melanoma, as well as a sophisticated antibody that will target cancers and lupus.

Developing such groundbreaking treatments is neither cheap nor easy. A mere five out of every 5,000 compounds devised will ever make it to clinical testing. The testing process itself takes, on average, at least seven years. And after all that, only one in five drugs tested on humans will ever make it to pharmacy shelves.

The biologic development process is, unsurprisingly, extremely expensive. Including the cost of drugs that fail, the average cost to bring a new drug to market is $1.2 billion. In 2011 alone, the biotechnology sector spent $49.5 billion in research and development. … (Source: MySA)

☞ Risk-based supply chain management means more audits for excipient firms

Regulatory pressure for risk-based supply chain management is increasing excipient suppliers' audit burden according to the team preparing to launch the 'excipact' certification scheme as an independent association.

The comments came from European Fine Chemicals Group (EFCG) vice chairman Frithjof Holtz, head of advocacy at Merck Millipore, who told attendees at CPhI in Frankfurt, Germany last week the economic burden extra audits places on suppliers and excipient users "*should not be underestimated*."

"*There are increasing expectations from regulators on ensuring the safety of the supply chain means more physical audits of manufacturers, suppliers and also distributors, warehouses, forwarders and so on*."

He cited –in Europe - the FMD which requires risk assessment for appropriate good manufacturing practices for excipients and moves to revise GMPs and – in the US – FDASIA's supplier registration requirement as examples of regulatory moves that have increased the audit burden. … (Source: In-Pharma)

☞ Vaccines Do Not Cover Most Common HPV Types in Black Women

The HPV subtypes that are most common in black women in the United States are not targeted by the currently available vaccines *Gardasil* and *Cervarix*, according to new research.

The findings suggest that current HPV vaccination will be less beneficial for black women in the US than for their white counterparts, said study coauthor Catherine Hoyo, PhD, MPH, of Duke University, in Durham, North Carolina. … (Source : Medscape)

http://www.ich.org/ http://www.picscheme.org/ http://www.ipec-europe.org

☞ Summary of ICH Q3D – Guideline for Elemental Impurities Draft Consensus Guideline

Within scope:

–New finished drug products (as defined in ICH Q6A and Q6B) and new drug products employing existing drug substances

–Drug products containing proteins and polypeptides (produced from recombinant or non-recombinant cell-culture expression systems), their derivatives, and products of which they are components (e.g. conjugates)

–Drug products containing synthetically produced polypeptides, polynucleotides, and oligosaccharides

Summary_FDA Draft Guidance (Q3D) (October 2013).pdf

EUROPEAN UNION

☞ Submission of comments on Revision 4 of the Guideline on the format and content of application for designation as orphan medicinal and on its transfer from one sponsor to another (ENTR/6283/00 Rev 4) and Revised Application form for orphan medicinal product designation

(Source: EC)

☞ Submission of comments on "Guideline on the format and content of applications for designation as orphan medicinal products and on the transfer of designations from one sponsor to another" (ENTR/6283/00 Rev 4; 12 June 2013) and Annex (Application Form for Orphan Medicinal Product Designation) (Source: EC) (Hoffman-La Roche)

☞ Submission of comments on ' Guideline on the format and content of applications for designation as orphan medicinal products and on the transfer of designations from one sponsor to another ' (ENTR/6283/00 Rev 4) (Source: EC, Novartis) (EC, SHIRE)

☞ Commission Européenne: Que signifie le triangle noir?

L'Union européenne (UE) a mis en place un nouveau moyen d'identifier les médicaments faisant l'objet d'une surveillance particulièrement étroite (Source: EC)

☞ Use of '-omics' technologies in the development of personalised medicine

Under the heading 'Towards more personalised medicines' in its Communication1 of 10 December 2008 on a Renewed Vision for the Pharmaceutical Sector, the Commission announced a report on the use of '-omics' technologies2 in pharmaceutical research and development.

This report, presented in the form of a staff working document, focuses on:

- the potential and issues with the use of -omics technologies in the research and development of personalised medicine and current EU research funding in the area;

- recent developments in EU legislation for placing medicinal products and medical devices on the market;

- factors affecting the uptake of personalised medicine in health care systems. … (Source : EC)

☞ Janssen files EMA marketing authorisation application for blood cancer medicine Ibrutinib

Janssen-Cilag (Janssen), a subsidiary of Johnson & Johnson pharmaceutical firm, has submitted marketing authorization application (MAA) to the European Medicines Agency (EMA) for the approval of once daily oral drug ibrutinib for the treatment of two forms of blood cancer.

The approval is intended to treat adult patients with relapsed or refractory chronic lymphocytic leukemia (CLL)/small lymphocytic leukemia (SLL) and or relapsed or refractory mantle cell lymphoma (MCL).

The company claims that ibrutinib is the first in a class of medicines called Bruton's tyrosine kinase (BTK) inhibitors.

According to the company, ibrutinib covalently bonds to BTK in malignant B cells, shutting down major proliferation and survival pathways. … (Source: PBR)

☞ Baxter files application to market hemophilia B vaccine Rixubis in Europe

Baxter has submitted a marketing authorization application (MAA) to the European Medicines Agency (EMA) for approval of Rixubis, recombinant factor IX for the treatment and prophylaxis of bleeding in patients of all ages with hemophilia B.

Hemophilia B is the second most common type of haemophilia and results from insufficient amounts of clotting factor IX, a naturally occurring protein in blood that helps to control bleeding.

The submission is based on results of research with hemophilia B patients previously treated with other therapies and is further supported by data secured from a study of 23 hemophilia B patients less than 12 years old. … (Source: PBR)

☞ EUnetHTA strengthens its position as the scientific and technical cooperation on HTA in Europe (Source: EUnetHTA)

European Medicines Agency

http://www.ema.europa.eu/ema/

Human medicines: Regulatory

http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/landing/human_medicines_regulatory.jsp&mid=WC0b01ac058001ff89

☞ New EMA guidance on development of antibacterials to help in the fight against multidrug-resistant pathogens

The European Medicines Agency (EMA) today released an Addendum to the guideline on the evaluation of medicinal products indicated for the treatment of bacterial infections. One of the most important aspects of the addendum is that it outlines a new approach facilitating the development of antibacterial agents targeted against multidrug-resistant (MDR) pathogens where patients have very limited or no remaining treatment options. It also gives guidance on data-gathering strategies to support the benefit-risk evaluation as part of the marketing-authorisation process for different indications.

This addendum complements the Guideline on evaluation of medicinal products indicated for treatment of bacterial infections. … (Source: EMA)

☞ Questions and Answers on Design Space Verification

Q&A - Design Space Verification - October 2013.pdf

☞ Amendments to the pharmacovigilance legislation: new notification requirements for marketing-authorisation holders and changes to scope of European safety referrals

Amendments of the European Union (EU) pharmacovigilance legislation that were adopted in October 2012 came into force on Monday 28 October 2013. These changes, which cover various aspects of the legislation, aim to further strengthen the protection of patient health by increasing the ability of the European medicines network to take prompt and appropriate regulatory action. … (Source: EMA)

☞ Meeting highlights from the Committee for Medicinal Products for Human Use (CHMP) 21-24 October 2013

This page provides an overview of the opinions adopted at the October 2013 meeting of the Committee for Medicinal Products for Human Use (CHMP) and other important outcomes.

Three new medicines recommended for approval

This month, the CHMP recommended the approval of **Opsumit**, an orphan medicine intended for the treatment of pulmonary arterial hypertension in adults.

The Committee gave a positive recommendation for **Brintellix** in the treatment of major depressive episodes in adults.

The generic medicine **Levetiracetam Hospira** also received a positive opinion for use in epilepsy. … (Source: EMA)

☞ EMA: How access to full clinical-trial data sets will benefit medicines developers (Source: EMA)

☞ European Medicines Agency advises on compassionate use of sofosbuvir (Source: EMA)

☞ First qualification opinion on a statistical methodology for dose finding released for public consultation (Source: EMA)

☞ EMA: Revised reflection paper on injection site residues: considerations for risk assessment and residue surveillance - Draft (Source: EMA)

☞ Concept paper on the revision of the Note for guidance on the approach towards harmonisation of withdrawal periods (Source: EMA)

☞ Comments invited on concept paper on the need to revise the guideline on medicines to treat Alzheimer's disease

The European Medicines Agency has released a concept paper on the need to revise the guideline on medicines for the treatment of Alzheimer's disease and other dementias for public consultation.

Comments should be sent by 31 January 2014 to cnswpsecretariat@ema.europa.eu, using the template provided. … (Source: EMA)

☞ The patient's voice in the evaluation of medicines

How patients can contribute to assessment of benefit and risk

The ultimate *raison d'être* of any medicine is to benefit patients. However, older and more paternalistic models of medicine often treated patients as a passive group who were to be given instructions but who should not be confused or worried by too much information. Although the best healthcare professionals have always recognised the importance of listening carefully to their patients, the idea that patients' knowledge, views and preferences were as significant as those of any other stakeholder in the healthcare process was not a standard part of this model. Over the past decades this has changed, as it has become increasingly clear that such a model is neither appropriate nor useful in a better connected and less deferential world.

The Workshop on the patient's voice in the evaluation of medicines brought together representatives of patients, consumers and healthcare professionals as well as the pharmaceutical industry and members of the Agency's scientific committees and staff.

Action points identified included the need to:

- identify where quantitative versus qualitative input is needed, and develop and validate new tools for eliciting values and preferences and representing benefit and risk; these tools need to take account of the way values vary between patients and can change during the patient journey;
- develop means for identifying and managing differences of view among patients, and between patients and other stakeholders;
- consider what training and support is needed to maximise patient involvement at all stages of the process for the full range of disease states, and who should be supplying these;
- further develop the role and timing of patient involvement in later, post-marketing stages of the product lifecycle (e.g. in signal assessment);
- identify and try to minimise legal, regulatory, financial and procedural barriers to patient involvement.

These action points will be considered as part of the on-going review of the existing formal framework of interaction between the Agency and patient and consumer organisations. This framework has been in place since 2005 and defines how the Agency interacts with patients and consumers.

EMA - Report - The patient's voice in the evaluation of medicines - 18Oct2013.pdf

☞ European Medicines Agency launches public catalogue of medicine shortages assessed by the Agency

The European Medicines Agency has launched a public catalogue that contains information on supply shortages of medicines.

The catalogue includes information on medicine shortages affecting more than one Member State and that have been assessed by the Agency.

The aim of the catalogue is to offer a reference point for stakeholders for up-to-date information on shortages that have been assessed by the Agency.

The catalogue provides:

- information on the reason of the shortage and the current status of the shortage (ongoing or resolved)
- information on the extent of the shortage;
- specific information for patients and healthcare professionals;
- links to relevant related documents.

Over the past few years, there have been a number of public-health crises caused by supply shortages of medicines as a result of manufacturing issues and good-manufacturing-practice (GMP) compliance problems.

Shortages can have important consequences for patients and healthcare professionals, such as the need to switch to an alternative treatment and the setting-up of priority-access programs.

The creation of this catalogue is part of an implementation plan developed by the Agency in 2012 to help the European medicines regulatory network deal with medicine supply shortages following manufacturing problems. This short- and medium-term plan includes a number of actions that aim to prevent, mitigate and manage shortages of medicines.

As part of these planned actions, the Agency held a workshop on the prevention of medicine shortages due to manufacturing and quality problems in October 2013. The workshop aimed to discuss how to improve existing risk-management strategies and how to mitigate the impact of shortages. A workshop report will be published shortly.

☞ European Medicines Agency meeting and holiday dates 2013 (Source: EMA)

☞ European Medicines Agency's Management Board supports plan to publish agendas and minutes of all committees (Source: EMA)

☞ Nomination au Comité des médicaments à usage humain de l'Agence européenne des médicaments

Le Dr Pierre Demolis, directeur de la direction des médicaments en oncologie, hématologie, immunologie, néphrologie de l'ANSM, membre du CHMP depuis 2007, a été élu à la vice-présidence du Comité des médicaments à usage humain de l'Agence européenne des médicaments (EMA) pour une durée de 3 ans.

HERBAL MEDICINES FOR HUMAN USE

http://www.ema.europa.eu/ema/index.jsp?curl=pages/medicines/landing/herbal_search.jsp&mid=WC0b01ac058001fa1d

CMDh
Co-ordination Group for Mutual Recognition and Decentralised Procedures – Human

http://www.hma.eu/cmdh.html

WHAT'S NEW: http://www.hma.eu/186.html

☞ Regulation (EC) No 1234/2008 on variations

The CMDh has adopted a new version of Chapter 7 (work-sharing) of the CMDh Best Practice Guide for the submission and processing of variations in the mutual recognition procedure. The document was updated to clarify that all Member States as proposed by the MAH for work-sharing procedures for purely national marketing authorisations should accept the submission of the variation application if the work-sharing fulfils the requirements for a work-sharing procedure. The revised Chapter 7 will be published on the CMDh website under "Procedural Guidance, Variation".

The CMDh has revised the Questions & Answers on variation. Questions No. 3.10 on deletion of a pharmaceutical form or strength and No. 4.15 on the introduction or update of the summary of the pharmacovigilance system and change in the QPPV, have been amended for clarification purpose. revised Questions & Answers document will be published on the CMDh website under "Questions and Answers, Variations".

CMDh - Q&A - Submission of variations - Oct 2013.pdf

☞ CMDh BEST PRACTICE GUIDE ON WORKSHARING

This guidance covers worksharing procedures for:

- a group of products from the same marketing authorisation holder[1] where none of the marketing authorisations is a centralised marketing authorisation. It may include marketing authorisations granted via MRP/DCP as well as purely national marketing authorisations or a mixture of MRP/DCP and purely national marketing authorisations.

- a purely national marketing authorisation held by the same marketing authorisation holder in more than one Member State.

In these cases, the competent authority of a Member State concerned chosen by the Coordination Group shall be the 'reference authority'. In case the worksharing procedure only contains products with the same RMS there is no need for the CMDh to choose the reference authority (see section 4 "Worksharing of MR/DC procedures with the same RMS").

CMDh - BEST PRACTICE GUIDE ON WORKSHARING Chapter 7 - October 2013 - track changes.pdf

☞ Pilot on work-sharing procedure for the assessment of Active Substance Master Files (ASMF)

The working group on Active Substance Master File procedures is actively preparing for the start of the pilot on work-sharing procedure for the assessment of ASMF. A meeting with representatives of Interested Parties has been organised in the margin of the CMDh meeting in order to discuss the pilot. The objective of the meeting was to present to Industry the procedures for request of an EU ASMF reference number and submissions of a new ASMF and to answer questions from Interested Parties.

Companies wishing to participate in the pilot will have to fill-in the EU AMSF number request form that will be published on the CMDh website under "CMD Working Parties/Working Groups, Working Group on Active Substance Master File Procedures". In order to facilitate the request of EU ASMF numbers, a dedicated list of contact persons has been set up that will be added to the published "Contact Points".

CMDh - EU_ASMF_number_request_form.docx

☞ "BLUE – BOX" REQUIREMENTS

CMDh - Blue Box requirements - October 2013.pdf

edqm European Directorate for the Quality of Medicines & HealthCare http://www.edqm.eu/en/edqm-homepage-628.html

☞ Council of Europe's European Directorate for the Quality of Medicines and Healthcare (EDQM) and European Medicines Agency joint meeting on raw materials used for the production of cell-based and gene-therapy products

REPORT symposium - raw materials - cell-based and gene therapy products.pdf

☞ Safety Data Sheets subscriptions and translations (Source: EDQM)

☞ Counterfeiting of medical products: the Council of Europe steps up action worldwide with the Medicrime Convention (Source: EDQM)

☞ Certification Monthly Report of Activities (Source: EDQM)

FRANCE

☞ Décret no 2013-935 du 18 octobre 2013 relatif aux modalités de déclaration de certaines contributions pharmaceutiques (Source: LegiFrance)

☞ Décret no 2013-923 du 16 octobre 2013 pris pour la transposition de la directive 2012/26/UE du 25 octobre 2012 modifiant en ce qui concerne la pharmacovigilance la directive 2001/83/CE instituant un code communautaire relatif aux médicaments à usage humain (Source: LegiFrance)

☞ Vente à l'unité des antibiotiques

L'Assemblée nationale a autorisé, dans le cadre du projet de loi de financement de la Sécurité sociale 2014, des expérimentations de vente à l'unité des antibiotiques, « lorsque leur forme le permet ».

Un décret fixera les conditions d'expérimentations qui dureront trois ans. (Source : Assemblee-nationale)

☞ André Choulika, chef du plan industriel sur les biotechs, mise tout sur la thérapie cellulaire

Pour ce pragmatique, pas question de multiplier les réunionites. Il a profité du dernier conseil d'administration de France Biotech pour arbitrer. "*Sachant qu'il n'y a pas beaucoup d'argent mis sur la table et que cela doit être un projet industriel, pas une usine à gaz, nous nous sommes concentrés sur un seule thématique*", confie André Choulika. Les traitements issus de la biologie de synthèse ont été écartés, au profit de la thérapie cellulaire. Un domaine émergent des biotechnologies qui constitue "*un vrai saut quantique : pouvoir corriger d'emblée la cellule du patient plutôt que lui donner un traitement palliatif*", estime Patrick Biecheler, associé en charge de la santé au cabinet Roland Berger. Dans lequel la France voit se structurer un centre d'excellence, avec la plateforme de production unique en Europe inaugurée en septembre par CellforCure, filiale du laboratoire pharmaceutique public LFB. … (Source : UsineNouvelle)

☞ Les investissements pharma s'effondrent en France

Voici une volée de chiffres qui va apporter de l'eau au moulin des industriels français de la filière pharmaceutique française, très remontés contre le PLFSS 2014 et la politique fiscale menée par le gouvernement qui, selon eux, compromettent gravement l'attractivité du territoire. Ainsi, selon l'Observatoire des investissements productifs créé par le **Leem** et le cluster **Polepharma** qui présentait hier ces données en avant-première, les investissements corporels bruts engagés en 2012 se sont élevés à 590,7 M€, soit une baisse… de 44 % en quatre ans. Environ 70 % de ce montant peut être attribué à cinq groupes seulement. *« Il est temps de sonner le tocsin »*, a souligné Pascal Le Guyader, directeur des affaires générales, industrielles et sociales du Leem à l'issue de cette présentation. Il a par ailleurs estimé que le solde net des emplois créés par la filière pourrait, en 2013, *« être négatif, probablement de l'ordre de – 1 % »*. … (Source: ActuLabo)

☞ Valorisation et modélisation médico-économique du couple Test diagnostique compagnon et Thérapie ciblée

Cette contribution a pour objectif de discuter de la démarche à suivre dans le cadre d'une évaluation médico-économique d'un couple test compagnon/thérapie ciblée en abordant les points méthodologiques clés à considérer dans ce type d'analyse.

Ce travail s'est structuré autour d'une analyse des données de la littérature et de la présentation d'un modèle conceptuel envisageable dans le cas d'une thérapie ciblée anti-cancéreuse et de son test compagnon prédictif de la réponse au traitement.

Bien que la cancérologie constitue le principal champ de réflexion de ce travail au travers des exemples cités et du cas d'étude, les couple(s) test(s) compagnon(s)/thérapie(s) ciblée(s) et plus largement la médecine personnalisée représentent un enjeu commun à de nombreuses aires thérapeutiques. … (Source : Leem)

☞ LEEM: Fiscalité des entreprises du médicament - La France accroît son décrochage avec les autres pays européens (Source: LEEM)

☞ Les contrats commerciaux liant les industriels du générique et les officines, plus transparents

Un article du projet de loi de financement de la Sécurité sociale (PLFSS) pour 2014 prévoit d'imposer aux industriels de déclarer les avantages commerciaux et financiers accordés aux pharmaciens. ... (Source : Daso Santé)

Quand les applications électroniques (e-apps) sont-elles des Dispositifs Médicaux ?
Le Cabinet WHITE-TILLET est spécialiste de la question et peut vous aider à y répondre ; le cas échéant, nous pouvons vous assister pour le marquage CE de votre application.

http://ansm.sante.fr/

☞ ANSM: Vigilances

Mise en place de la nouvelle législation en pharmacovigilance, quel bilan un an après? (Source: ANSM)

☞ Textes publiés en 2013 concernant les médicaments

Médicaments, médicaments combinés de thérapie innovante, préparations magistrales, hospitalières, officinales, APSI (allergènes préparés spécialement pour un individu) substances stupéfiantes, psychotropes ou autres substances vénéneuses, insecticides, acaricides et antiparasitaires à usage humain, huiles essentielles, plantes médicinales, matières premières à usage pharmaceutiques, pharmacopée. … (Source : ANSM)

☞ L'ANSM a réuni tous ses agents pour préparer l'avenir - Point d'information

L'Agence nationale de sécurité du médicament et des produits de santé a rassemblé, le 15 octobre 2013, l'ensemble de ses agents pour une journée de partage et d'échanges, plus d'un an après sa mise en place et 20 ans après la création de la première agence du médicament. Après une matinée réservée aux collaborateurs internes qui a permis de dresser un premier point d'étape sur les nouveaux modes de fonctionnement de l'agence et sur sa stratégie d'action pour répondre aux enjeux qui lui ont été assignés, l'Agence a accueilli l'après-midi des acteurs de la santé qui ont fait part de leur analyse et de leur vision sur les évolutions en cours en matière de transparence, d'indépendance, d'information et de surveillance des médicaments. … (Source: ANSM)

Le Cabinet WHITE-TILLET s'est entouré de juristes de haut niveau pour vous aider à valider la publicité et la promotion de vos médicaments. Leur expertise se combine à notre expérience réglementaire et à notre maîtrise de la méthodologie clinique. Contactez-nous pour le reviewing de vos documents publicitaires ou promotionnels!

☞ Valdoxan (agomélatine): Ajout d'une nouvelle contre-indication et rappel sur l'importance de la surveillance de la fonction hépatique - Point d'information (Source: ANSM)

☞ Caustinerf Arsenical et Yranicid Arsenical, pâtes pour usage dentaire : un signal de génotoxicité est susceptible de remettre en cause le rapport bénéfice/risque de ces spécialités - Point d'information (Source:

ANSM)

☞ Ce qu'il faut savoir avant de commencer un traitement par isotrétinoïne orale (Source: ANSM)

☞ Spécialités à base de fer pour injection intraveineuse: une utilisation réservée aux établissements de santé en raison du risque de réactions graves d'hypersensibilité - Point d'information (Source: ANSM)

☞ Déclarer un effet indésirable: quoi de neuf pour les professionnels de santé et les patients? - Point d'Information (Source: ANSM)

Le Cabinet WHITE-TILLET a plus de 20 ans d'expérience et d'expertise dans le domaine des dossiers d'AMM. Nous maîtrisons l'eCTD. Par notre structure et notre réseau (cabinet associé au UK, réseau international), nous maîtrisons les procédures et assurons un suivi efficace. Confiez-nous vos dossiers d'AMM ou de variations!

HAUTE AUTORITÉ DE SANTÉ http://www.has-sante.fr/portail/jcms/j_5/accueil

☞ FICHES DE BON USAGE (Source : HAS)

☞ SYNTHÈSES D'AVIS SUR LES MÉDICAMENTS (Source : HAS)

☞ Label de la HAS - Troubles du Comportement chez les Traumatisés Crâniens: Quelles options thérapeutiques?

Les troubles du comportement des victimes de traumatisme crânien constituent la séquelle majeure chez ces blessés. Les troubles du comportement ont des conséquences néfastes multiples impliquant les familles, les soignants, et nombre d'autres professionnels (magistrats, avocats, assureurs etc.). Le présent travail a pour objectifs :

- d'organiser la démarche de soins dont une meilleure information des intervenants occasionnels,
- de fournir un guide pratique de prise en charge pour le praticien,

- d'améliorer l'efficience des différentes modalités thérapeutiques : traitements médicamenteux et non médicamenteux, stratégie thérapeutique, hospitalisation, suivi ambulatoire, insertion professionnelle y compris en milieu adapté.

… (Source: HAS)

☞ Maladie d'Alzheimer et maladies apparentées: diagnostic et prise en charge de l'apathie - Note de cadrage

Cette note de cadrage présente le projet de recommandations de bonne pratique sur le thème « diagnostic et prise en charge de l'apathie chez les patients atteints de maladie d'Alzheimer ou de maladies apparentées » qui est en cours de réalisation par la HAS.

Les recommandations sur la prise en charge des troubles du comportement perturbateurs chez les patients atteints de maladie d'Alzheimer ou de maladies apparentées publiées par la HAS en 2009 ont exclu les troubles du comportement déficitaires ou de retrait telle que l'apathie, également fréquente au cours de ces maladies. L'élaboration de ces recommandations professionnelles entre dans le cadre du Plan Alzheimer 2008-2012. … (Source: HAS)

☞ HAS: RAPPORT D'EVALUATION TECHNOLOGIQUE - Utilité clinique du dosage de la vitamine D (Source: HAS)

Ministère des Affaires Sociales et de la Santé **CEPS**

http://www.sante.gouv.fr/comite-economique-des-produits-de-sante-ceps.html

Le Cabinet WHITE-TILLET a près de 30 ans d'expérience et d'expertise dans le domaine du remboursement des médicaments, incluant la maîtrise de la méthodologie clinique. La rédaction de ces dossiers est un art complexe. Les conséquences pour les firmes peuvent être cruciales. Confiez-nous vos dossiers de remboursement !

EUROPE

MHRA http://www.mhra.gov.uk/

☞ MHRA: Department of Health (DoH) appoints new Chair of the British Pharmacopoeia Commission (Source: MHRA)

☞ Antimicrobial prescribing and stewardship competencies

The goal is to improve the quality of antimicrobial treatment and stewardship and so reduce the risks of inadequate, inappropriate and ill-effects of treatment. This will improve the safety and quality of patient care, and make a significant contribution to the reduction in the emergence and spread of antimicrobial resistance. Antimicrobial stewardship is an important element of the UK five-year antimicrobial resistance strategy (1) and the Chief Medical Officer's annual report (2).

Antimicrobial resistance is a global public health issue driven by the overuse of antimicrobials and inappropriate prescribing. The increase in resistance is making antimicrobial agents less effective and contributing to infections that are hard to treat. The number of infections due to multi-drug resistant organisms is growing, however, the number of new antibiotics in the pieline is extremely limited.

Antimicrobial stewardship initiatives aim to improve the prescribing of all agents, whether they target bacterial, viral, fungal, mycobacterial or protozal infections.

Antibiotic resistance is of particular threat to children, older people and those with weakened immune systems. Effective antibiotics have revolutionised many treatments, such as those for cancer, allowing more aggressive therapy to be used and consequently leading to higher survival rates. Nevertheless, an increase in infections that are more difficult to treat with antibiotics affects everyone, not just vulnerable groups. Bacterial resistance potentially complicates the management of every infection, no matter how mild they may be at the time of first presentation.

Educating the public and clinicians in the prudent use of antimicrobials as part of an antimicrobial stewardship programme is of paramount importance to preserve these crucial treatments and to help control resistance. Improving surveillance, and infection prevention and control are other key strategies.

UK - DH - Antimicrobial prescribing and stewardship compentencies - October 2013.pdf

☞ U.K. Drug Regulator Recalls 5 Drugs Made by India's Wockhardt (Source: WSJ)

☞ UK health research body backs trial data disclosure & access to patient data (Source: Clinica)

☞ Information sent to healthcare professionals in October about the safety of medicines

Copies of letters sent to healthcare professionals in October 2013, to inform of new safety information and advice. … (Source: MHRA)

☞ Ten years and beyond

In the last ten years, the Agency expanded its offerings including:

- licensing decisions on whether to grant authorisations to place medicines on the market
- authorisation and inspection of clinical trials of medicines
- new procedures for authorising medicines intended to be marketed across Europe

Recently, National Institute for Biological Standards and Control (NIBSC) join the Agency. NIBSC is responsible for producing over 90% of the International Standards used to assure the quality of biological medicines. … (Source: MHRA)

NHS National Institute for Health and Clinical Excellence http://www.nice.org.uk/

☞ Following simple steps can help reduce surgical-site infections, saving lives and money, says NICE in new standards

Surgical site infection is a type of healthcare-associated infection in which a surgical incision site becomes infected after a surgical procedure. Surgical site infections have been shown to account for up to 16% of all healthcare-associated infections. The rate of surgical site infection varies depending on the type of procedure, with rates of over 10% for large bowel surgery, and less than 1% for orthopaedic procedures. Surgical site infections can often be prevented with appropriate care before, during and after surgery. If an infection does develop, the correct treatment will minimise complications resulting from the infection.

The NICE quality standard is based on the NICE guidance on both surgical site infection and healthcare-associated infections. … (Source: NICE)

☞ NICE draft "yes" for Astellas' prostate cancer drug

The National Institute for Health and Care Excellence (NICE) has issued draft guidance recommending Astellas Pharma's Xtandi (enzalutamide) for treating hormone relapsed metastatic prostate cancer.

Xtandi is an effective treatment and, as it can be taken orally, it allows patients to be treated at home, said Professor Carole Longson, director of NICE's Centre for Health Technology Evaluation.

Xtandi works in a different way to other drugs currently available for prostate cancer treatment. NICE's draft guidance recommends it as an option for treating hormone relapsed prostate cancer in adults, only if their disease has progressed during or after one docetaxel-containing chemotherapy regimen and if the manufacturer provides it with the discount agreed in the patient access scheme (PAS).

NICE says that its independent appraisal committee had heard that, although both Xtandi and Johnson & Johnson's prostate cancer drug Zytiga (abiraterone) are oral treatments, only Xtandi can be taken on a full stomach, making it more convenient to take. The panel was also told that Xtandi can help control the cancer longer because there is no need to reduce the dose to prevent liver toxicity, as with Zytiga.

The draft guidance has been welcomed by Prostate Cancer UK, which points out that Xtandi is one of the few treatments shown to extend the lives of men with advanced prostate cancer. … (Source : PharmaTimes) (NICE)

☞ NICE says yes to eye condition treatment in draft guidance

NICE has published draft guidance recommending ocriplasmin (Jetrea, ThromboGenics) as an option for treating some adults with the rare eye condition, vitreomacular traction.

Vitreomacular traction occurs when the vitreous, the gel-like substance in the eye, pulls abnormally on the retina, the light-sensitive layer of tissue at the back of the inner eye, which is responsible for processing

visual images. The pulling of the gel disturbs the retina, causing swelling and distorted vision, and sometimes a hole in the macular area. It can occur as a result of ageing.

NICE has **recommended ocriplasmin** as an option for treating vitreomacular traction in adults, including when associated with a macular hole with a diameter of 400 micrometres or less, only if they have severe symptoms and an epiretinal membrane is not present. … (Source: Nice)

☞ NICE: Choroidal neovascularisation (pathological myopia) - ranibizumab: final appraisal determination (Source: NICE)

☞ NICE: Non Hodgkin's lymphoma (relapsed refractory) - pixantrone monotherapy: appraisal consultation 2 (Source: NICE)

☞ NICE rejects J&J's Zytiga as too expensive

The National Institute for Health and Clinical Excellence issued draft guidance recommending against Zytiga use, saying that the drug doesn't work well enough to justify its price. And that's after J&J offered a discount to help sway the agency in its favor. … (Source : FiercePharma)

IRISH MEDICINES BOARD http://www.imb.ie/

☞ IRISH MEDICINES BOARD - GUIDE TO AMENDMENT AND RENEWAL APPLICATIONS FOR PROJECTS REGULATED BY DIRECTIVE 2010/63/EU AND S.I. NO. 543 OF 2012 (Source: IMB)

☞ IMB: Guide to Interchangeable Medicines (Source: IMB)

afmps agence fédérale des médicaments et des produits de santé http://www.fagg-afmps.be/fr/

☞ Pharmacovigilance : Nouvelle réglementation en matière de pharmacovigilance pour les médicaments à usage humain (Source : AFMPS)

http://www.bfarm.de/DE/Home/home_node.html

http://www.agenziafarmaco.gov.it/en

http://www.aemps.gob.es/en/home.htm

http://www.legemiddelverket.no/English/Sider/default.aspx

http://www.lakemedelsverket.se/english/

☞ **Health system review**

Health system review - Austria.pdf

http://www.eum.hu/about-us/the-ministry/ministry-of-health

http://www.swissmedic.ch/index.html?lang=fr

☞ **Fake drugs intercepted by Swiss customs** (Source: SwissInfo)

☞ **DHPC – Erivedge® (vismodegib): prolongation de 7 mois à 24 mois de la période pendant laquelle une contraception est recommandée après la fin du traitement par Erivedge chez les femmes en état de procréer** (Source: SWISSMEDIC)

☞ **Toxine botulique de type A: médicaments autorisés et indications, mode d'emploi correct, risques et precautions** (Source: SWISSMEDIC)

Les Bonnes Pratiques de Fabrication (GMP) et les Bonnes Pratiques Cliniques (GCP) sont au cœur de nos préoccupations et dans notre champ de compétence. N'hésitez pas à venir vers nous pour réaliser vos audits. Nous avons un réseau de des correspondants locaux en Asie et aux Etats-Unis.

RUSSIA & RELATED COUNTRIES

Ministry of Healthcare of the Russian Federation

http://government.ru/eng/power/23/

Ministry of Health of Ukraine

http://www.kmu.gov.ua/control/en/publish/article?art_id=88456

☞ Health system review

Health system review - Belarus.pdf

NORTH AMERICA

http://www.fda.gov/

☞ FDA: Guidance for Industry - Chronic Hepatitis C Virus Infection: Developing Direct-Acting Antiviral Drugs for Treatment - Revision 1 (Source: FDA)

☞ FDA: Guidance for Industry - Acute Bacterial Skin and Skin Structure Infections: Developing Drugs for Treatment (Source: FDA)

☞ FDA: Guidance for Industry - Q4B Evaluation and Recommendation of Pharmacopoeial Texts for Use in the ICH Regions Annex 14 - Bacterial Endotoxins Test General Chapter (Source: FDA)

☞ FDA: DRAFT CONSENSUS GUIDELINE GUIDELINE FOR ELEMENTAL IMPURITIES Q3D (Source: FDA)

☞ Draft Guidance on Iron Sucrose

FDA - Draft Guidance on Iron Sucrose.pdf

☞ FDA approves extended-release, single-entity hydrocodone product (Source: FDA)

☞ Statement on Proposed Hydrocodone Reclassification from Janet Woodcock, M.D., Director, Center for Drug Evaluation and Research (Source: FDA)

☞ FDA to complete phase-out of chlorofluorocarbon inhalers (Source: FDA)

☞ FDA awards 15 grants to stimulate drug, device development for rare diseases (Source: FDA)

☞ FDA: Draft Guidance for Industry: Use of Nucleic Acid Tests to Reduce the Risk of Transmission of West Nile Virus from Donors of Human Cells, Tissues, and Cellular and Tissue-Based Products (HCT/Ps) (Source: FDA)

☞ FDA Report Outlines Approach to Personalized Medicine

The report, *Paving the Way for Personalized Medicine: FDA's Role in a New Era of Medical Product Development*, outlines the fundamental ways in which the FDA has modified its traditional approaches to drug and device regulation in the new era of products that are tailored toward specific patient subtypes, rather than broad diagnostic groups.

"We're very, very excited about this report because I think it captures the broad context of what's happening in science and medicine today and the role of the FDA as we enter the era of personalized medicine, and for us, personalized medical product development," FDA commissioner Margaret A. Hamburg, MD, said in a press briefing held at the FDA headquarters Monday. … (Source: Medscape)

☞ Study questions FDA's shorter drug approval times

Study authors Thomas Moore of the Institute for Safe Medication Practices and Dr Curt Furberg, a professor at Wake Forest School of Medicine, examined the development times, clinical testing and risks associated with 20 new drugs approved in 2008. Eight were given expedited review and 12 standard review.

It found that expedited drugs underwent a median of 5.1 years of clinical testing before being approved, compared with 7.5 years for those that underwent a standard review. But in many cases safety monitoring trials that were supposed to be conducted after the products were approved were either not conducted, not completed, or not submitted to the FDA. … (Source: Reuters)

☞ FDA helps generic drugmakers get copies of Glaxo's Advair to market

GlaxoSmithKline's asthma drug Advair is hard to copy. The British pharma ($GSK) has said it time and again, and recently, generics giant Teva backed up that claim, saying producing a generic would be too difficult before 2018. Some companies have given up on generic Advair, while others have shied away altogether despite the substantial sales up for grabs. But what if generics makers had some help--and an expedited review process--from the FDA?

According to Leerink Swann analyst Jason Gerberry, that's exactly what's in the works. At this week's Generic Pharmaceutical Association (GPhA) conference, the agency announced plans to aim for a 10-month review on copies of complex drugs like Advair. It also said it's working with those companies looking to produce a rival to make sure they're on the right track. … (Source: FiercePharma)

☞ Novartis Group calls on FDA to maintain the well-established naming policy for all biologics to help ensure patient safety

Novartis announced today it has filed a Citizen Petition with the US Food and Drug Administration (FDA), urging the Agency to require that a biosimilar share the same INN as the reference product.

Novartis files Citizen Petition with FDA, urging uniform approach to use of international nonproprietary names (INN) for all biologic medicines

A modified INN for biosimilars would impede their ability to compete fairly in the marketplace, create confusion and limit patient access to these critical medicines

Novartis is confident in the FDA's ability to ensure safety and efficacy of all biologics, including biosimilars, through its well-established review process

Novartis argues that changing the well-established convention that the INN describe the active ingredient would undermine the safe and rational use of all biologics. In its petition, the company also highlights that 'assigning different INNs to biosimilars would introduce unnecessary confusion into the healthcare system and could unintentionally communicate increased caution, unfounded risk, or other regulatory reservations that are purely hypothetical.' … (Source: PMPNews)

☞J&J's Zytiga gets expanded approval that could double sales

The FDA on Monday said it approved Zytiga for treatment in men with late-stage, prostate cancer even before they receive chemotherapy. A study found that it reduced tumor growth and could extend life expectancy about 5 months. … (Source : FiercePharma)

☞ FDA approves Roche leukemia drug Gazyva

U.S. regulators said on Friday they approved a new treatment from Roche Holding AG for patients with chronic lymphocytic leukemia (CLL) who have not previously been treated for one of the most common forms of blood cancer. … (Source: Reuters)

USA

☞ BIO calls for different names for biosimilars, branded biotech drugs

Like their pharmaceutical counterparts, branded biotech drugs carry both a brand name and a generic chemical name, such as the autoimmune drug Enbrel, made by Amgen and Pfizer, known generically as etanercept. By law, generic pharmaceutical drugs are chemically identical to branded drugs and use the same generic names, and the companies wishing to make follow-on biologics, or biosimilars, want the same policy for their products.

But biotech companies say that because biosimilars are made from different cell lines from branded biologics, they are only similar rather than identical, and thus their generic names should be different, such as carrying a prefix. … (Source : DrugStoreNews)

pcori http://www.pcori.org/

☞ PCORI Launches Community-Building "Pipeline to Proposal" Awards

(Source: PCORI)

☞ Harold Sox, MD, to Serve as Senior Adviser to Patient-Centered Outcomes Research Institute (Source: PCORI)

☞ PCORI and AHRQ Partner on Request for Applications to Study Treatments for Uterine Fibroids (Source: PCORI)

AHRQ Agency for Healthcare Research and Quality
Advancing Excellence in Health Care http://www.ahrq.gov/

☞ AHRQ: Letters of Intent Due November 15 for Uterine Fibroid Project

(Source: AHRQ)

INSTITUTE OF MEDICINE
OF THE NATIONAL ACADEMIES http://www.iom.edu/

SANTE/HEALTH CANADA

http://www.hc-sc.gc.ca/index-fra.php#tabs1_3

☞ TPD: Guidance Document - Acetylsalicylic Acid Labelling Standard (Source: HC-SC)

☞ Health Canada is pleased to announce the release of the revised Post-Notice of Compliance (NOC) Changes - Quality Guidance (Source: HC-SC)

☞ CADTH : CDR Update — Issue 95 (Source: CADTH)

☞ Health Canada: Therapeutic Products Directorate Statistical Report 2012/2013 for the Patented Medicines (Notice of Compliance) Regulations and Data Protection (Source: HC-SC)

☞ CADTH: High-Sensitivity Cardiac Troponin for the Rapid Diagnosis of Acute Coronary Syndrome in the Emergency Department (Source: CADTH)

LATIN AMERICA

SSA http://www.salud.gob.mx/

☞ Faes Farma sets up JV in Mexico

Spain's Faes Farma is looking to expand in Latin America by setting up a joint venture with Mexico's Laboratorios Senosiain.

The 50:50 JV will be called MIT Farma and is an extension of the companies' 15-year relationship which has seen Senosiain sell the Bilbao-based firm's vasoproective product hidrosmine.

Faes says "we are convinced that Senosiain "is the best possible partner", in Mexico where it is the leading domestic pharmaceutical company and the fifth biggest drugmaker, including multinationals. … (Source: PharmaTimes)

National Health Surveillance Agency http://portal.anvisa.gov.br/wps/portal/anvisa/home

☞ Anvisa Sees Sectoral Agreements as New Form of Regulation (Source: ANVISA)

☞ RPT-Brazil to produce measles/rubella vaccine for poor countries

Brazil's top biomedical research and development center announced plans on Monday to produce a combined measles and rubella vaccine for developing countries, mainly in Africa.

The first Brazilian vaccine developed specifically for export will be made by Bio-Manguinhos, a unit of the Oswaldo Cruz Foundation (Fiocruz), in partnership with the Bill & Melinda Gates Foundation. … (Source: Reuters)

AFRICA

☞ UEMOA - UNION ECONOMIQUE ET MONETAIRE OUEST AFRICAINE

http://www.uemoa.int/Pages/Home.aspx

☞ REGLEMENT N°02/2005/CM/UEMOA RELATIF A L'HARMONISATION DE LA REGLEMENTATION PHARMACEUTIQUE DANS LES ETATS MEMBRES DE L'UEMOA (Source: UEMOA)

☞ REGLEMENT N° 06/2010/ CM/ UEMOA RELATIF AUX PROCEDURES D'HOMOLOGATION DES PRODUITS PHARMACEUTIQUES A USAGE HUMAIN DANS LES ETATS MEMBRES DE L'UEMOA (Source: UEMOA)

☞ Fiscalité des médicaments, consommables et équipements médicaux dans les pays membres de l'UEMOA (Source: Cerdi)

☞ L'Afrique de l'Ouest: des opportunités d'affaires à découvrir (Source: SlideShare)

https://www.dphm.ci/fr/dpm-c%C3%B4te-divoire-3

L'arrêté **N° 297 MSP/ CAB/ DGS/ DPM du 13 DEC 2006** fixe l'organisation, les attributions et le fonctionnement de la Direction de la Pharmacie et du Médicament en abrégé (DPM), conformément au **decrét N° 2006-33 du 08 mars 2006**, portant organisation du Ministère de la Santé et de l'Hygiène Publique.

La **Direction de la Pharmacie et du Médicament** , en abrégé, **DPM**, exerçant sous l'autorité de la Direction Générale de la santé, a pour missions d'élaborer, de mettre en œuvre et de veiller à l'application de la politique pharmaceutique nationale ;

A ce titre, elle est chargée :

- **De l'élaboration** des projets de textes législatifs et réglementaires en matière d'enregistrement de médicaments y compris des substances vénéneuses,des produits diététiques, cosmétiques et d'hygiène dans les secteurs publics et privés ;
- **De l'application** des Conventions et Traités internationaux relatifs aux stupéfiants et aux substances psychotropes ;
- **De la réglementation** des professions de pharmacie et de laboratoires d'analyses médicales ;
- **De l'établissement** et **de l'entretien** des relations avec les organisations professionnelles de pharmacie et de laboratoires d'analyses médicales ;
- **De l'organisation** de la pharmacovigilance ;
- **De l'organisation** de la lutte contre le trafic illicite de médicaments, stupéfiants et substances psychotropes ainsi que de la participation à la lutte contre la toxicomanie ;
- **De la promotion** et de la mise en œuvre du plan de développement de l'industrie pharmaceutique ;
- **Du secrétariat** de divers commissions notamment la commission de programmation des créations, des transferts, des gérances et des ventes d'officine de pharmacie et de laboratoires d'analyses médicales ; la commission nationale de thérapeutique ; la commission nationale de pharmacovigilance ; la commission d'enregistrement des médicaments ; la coordination des pays de la zone franc et les pays associés sur la politique du médicament.

☞ Promotion de l'Industrie Pharmaceutique (Source : DPHM)

☞ Pharmacovigilance et Lutte contre les Médicaments Illicites (Source: DPHM)

AUSTRALIA – NEW ZELAND

http://tga.gov.au/

☞ Biosimilar medicines - information for health professionals (Source: TGA)

☞ Consultation: Invitation for public comment - ACCS and joint ACCS/ACMS meetings, November 2013 (Source: TGA)

☞ Macutec - Stiltec Pty Ltd - Complaint No. 2011-11-017

Background: Regulation 9 of the Therapeutic Goods Regulations 1990 (the Regulations) permits the Secretary of the Department of Health (the Secretary) or her delegate to order a person, such as the advertiser of therapeutic goods, to undertake certain actions related to the advertising of therapeutic goods. Such an order can only be made on the recommendation of the Complaints Resolution Panel (the Panel), which is a statutory committee that examines complaints about advertisements for therapeutic goods.

On 21 August 2013, the TGA delegate of the Secretary (the Delegate) made an order in relation to Stiltec Pty Ltd about an internet advertisement at www.macutec.com.au regarding the product, Macutec. The order was made following a recommendation by the Panel on 15 August 2012 in relation to a complaint (No. 2011-11-017) made on 22 November 2011. The recommendation was made because Stiltec Pty Ltd had not fully complied with the Panel's determination issued on 15 June 2012. … (Source: TGA)

☞ Fifty new drugs listed on PBS

Fifty new and amended medicines have been added to the Pharmaceutical Benefits Scheme (PBS), including cancer drugs.

Health Minister Peter Dutton says it means about 230,000 people can receive treatments they might not otherwise have been able to afford.

The new listings include a ground-breaking treatment for melanoma skin cancer.

Dabrafenib, sold as Rafinlar, is the first melanoma medicine that targets a genetic mutation present in about half of all melanoma cases.

Mr Dutton says the genetic testing needed to determine eligibility for the medicine will also be subsidised, benefiting more than 800 Australians. … (Source: SMH)

☞ Role of the Advisory Committee on Prescription Medicines (ACPM) in the TGA's regulatory decision making process (Source: TGA)

☞ TGA presentations given at the complementary medicines road shows, July - August 2013 (Source: TGA)

☞ DSM opens Australia biologics plant

The contract manufacturing arm of the Dutch-based Royal DSM officially opened the $65 million facility Wednesday. The first custom mammalian-based biopharmaceutical manufacturing facility in Australia, it is a pet project of Australia's $345 million Translational Research Institute, which is being built to attract medical research to Australia. The Dutch company has gotten support from the governments of Queensland and the Commonwealth to build the plant. … (Source: FiercePharmaManufacturing)

ANZTPA http://www.anztpa.org/

INDIA - PAKISTAN & ASIA

China SFDA | Hong Kong MDCO & PSDH | India CDSCO | Japan MHLW | Korea KFDA | Malaysia MOH | Philippines DOH | Singapore HSA | Taiwan TFDA | Thailand FDA | Vietnam MOH

Pharmaceuticals and Medical Devices Agency, Japan

http://www.pmda.go.jp/english/

☞ The PMDA publishes a list of new drugs which are unapproved in Japan but approved in the USA and the EU

The following drug types are in scope of this list; USA: NDA Chemical Types 1 （New molecular entity (NME) and Biologics license application (BLA); EU: New Active Substance (NAS)

Medicines not approved in Japan but approved in EU or US.xls

☞ B-MS files first all-oral, interferon-free HCV drug in Japan

Bristol-Myers Squibb Co has filed an all-oral combination in Japan for hepatitis C, seeking "the world's first interferon- and ribavirin-free treatment regimen" for the disease.

The submission with Japan's Pharmaceutical and Medical Devices Agency is for daclatasvir, a NS5A inhibitor and the protease inhibitor asunaprevir. It is based on results from a Phase III study demonstrating that the combo achieved an overall sustained virologic response 24 weeks after the end of treatment of 84.7% in Japanese patients. … (Source: PharmaTimes)

☞ Bristol seeks Japan approval of all-oral hepatitis C treatment

The submission with Japan's Pharmaceutical and Medical Devices Agency marks the first time that any drugmaker has filed for approval of a hepatitis C treatment regimen that does not include either of the standard older treatments - the injected, difficult-to-tolerate interferon, or ribavirin, a pill. … (Source: Reuters)

http://eng.sfda.gov.cn/WS03/CL0755/

☞ China Issues Revised GSP for Cold Chain Quality Control (Source: SFDA)

☞ CFDA Releases New Rules Governing Regulatory Process (Source: SFDA)

☞ GSK's Chinese executives, but not company, likely to face charges in China - sources

Chinese police investigating allegations of widespread corrupt practices at GlaxoSmithKline Plc (GSK) are likely to charge some of its Chinese executives but not the British drugmaker itself, legal and industry sources said. … (Source: Reuters)

Food and Drug Administration - Department of Health

http://www.taiwan.gov.tw/ct.asp?xItem=25613&ctNode=1970&mp=1001

KFDA

http://www.kfda.go.kr/eng/index.do;jsessionid=8WaGRaioTcYSanehB1hMj6KOHjYV58zMGvaefbMlRWUQqdgxsIWA05GwBX1zZoJG

☞ Samsung BioLogics signe un partenariat de fabrication stratégique avec Roche

Samsung BioLogics a annoncé aujourd'hui la signature d'un accord de fabrication stratégique à long terme entre Samsung BioLogics et F. Hoffmann-La Roche. Les termes de cet accord prévoient la fabrication par Samsung des médicaments biologiques commerciaux et exclusifs de Roche dans ses deux installations de fabrication situées à Incheon, en Corée du Sud, dont l'une est en construction. Les conditions de l'entente, y compris les modalités financières et les produits qui seront fabriqués, ne seront pas dévoilées. … (Source : PRnewswire)

☞ WuXi adds two 2000-L bioreactors to Shanghai facility

WuXi PharmaTech (NYSE: WX), a leading pharmaceutical, biotechnology and medical device research and development outsourcing company with operations in China and the United States, announced today that it had completed a cell culture capacity expansion, including two 2000L disposable bioreactors that are ready for cGMP manufacturing. Previously WuXi AppTec had built a state-of-the-art cGMP biologics manufacturing facility with two cell culture suites containing a 500L and a 1000L disposable bioreactor, respectively. As a result of this new expansion, WuXi AppTec operates the largest biologics facility with disposable bioreactors in China and the largest disposable bioreactor in the world. The facility has passed GMP audits from global clients and an audit by former U.S. FDA biologics inspectors. … (Source: FiercePharmaManufacturing)

HSA http://www.hsa.gov.sg/publish/hsaportal/en/home.html#page=tab1

CDSCO http://www.cdsco.nic.in/

☞ India's health ministry directed to re-evaluate 157 clinical trials (Source: MedCityNews)

☞ After price cuts, big pharma companies focussing on brands, distribution

Big pharmaceutical companies' profit margins may be under pressure because of a government-induced fall in prices of dozens of medicines, but they could end up with a larger share of the market at the expense of small-and-mediumsized drug firms.

- Given the narrowed-down price differential between the prices of their drugs and those of small and medium firms, big pharmaceutical companies are now focussing on their brands and strengthening their

distribution setup. … (Source: TheEconomicTimes)

☞ Department of Pharmaceuticals rejects drug price review pleas of DRL, Abbott

The Department of Pharmaceuticals has rejected a review petition filed by leading drug makers, including Dr Reddy's Laboratories (DRL) and Abbott Healthcare, on ceiling of prices on their products.

While Abbott Healthcare filed the petition against the fixing of ceiling price of its Phenobabitone tablets--60mg and 30 mg--and Promethazine Injection, 25mg/ml, DRL opposed fixing of the ceiling price of Omeprazole 20 mg capsules. … (Source: TheEconomicsTimes)

☞ India slaps $787 per tn anti-dumping duty on Chinese paracetamol

India has imposed anti-dumping duty of $787 per tonne on import of Paracetamol, a widely used medicine, from China for five years to protect interest of domestic players from the cheap shipments.

"The anti-dumping duty imposed (on Paracetamol) under this notification shall be effective for a period of five years...," said the Central Board of Excise and Customs (CBEC) in the Revenue Department. … (Source: EconomicTimes)

☞ Patent office rejects BDR Pharma's compulsory licensing application

The Patent Office rejected the compulsory licensing application of Mumbai-based BDR Pharmaceuticals to make a generic version of US drug maker Bristol-Myers Squibb's anticancer drug Dasatinib, sold under the brand name Sprycel.

The ruling comes after India last year issued its first compulsory licence to Natco Pharma to manufacture the generic version of German drug maker Bayer's kidney cancer drug Nexavar. … (Source: EconomicTimes)

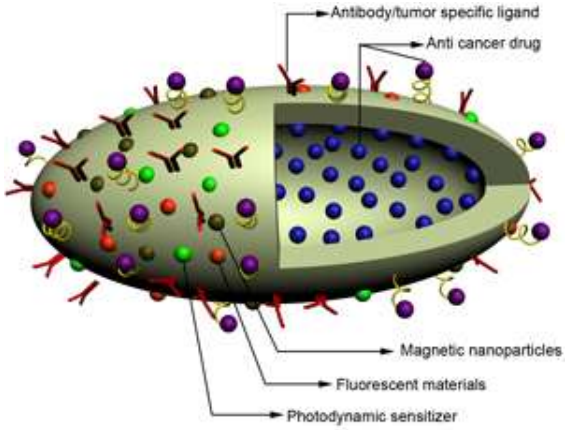
RESEARCH & DISCOVERY / BUSINESS DEVELOPMENT

☞ Drug Development Lags for Neglected Diseases

A new study published in *The Lancet Global Health* highlights what its authors call a 'fatal imbalance' in research and development of treatments for the world's poorest patients.

The authors acknowledge that pharmaceutical and biotechnology companies have little financial incentive to invest R & D funds in finding treatments or cures for neglected diseases, and point to a failure of public policy to encourage them. They conclude, "Despite substantial political attention towards the burden of neglected diseases, we detected no evidence of a substantial improvement in research and development activity compared with previous decades." … (Source: VOA)

☞ UC Develops Unique Nano Carrier to Target Drug Delivery to Cancer Cells



A unique nanostructure developed by a team of international researchers, including those at the University of Cincinnati, promises improved all-in-one detection, diagnoses and drug-delivery treatment of cancer cells.

The first-of-its-kind nanostructure is unusual because it can carry a variety of cancer-fighting materials on its double-sided (Janus) surface and within its porous interior. Because of its unique structure, the nano carrier can do all of the following:

- **Transport cancer-specific detection nanoparticles and biomarkers to a site within the body**, e.g., the breast or the prostate. This promises earlier diagnosis than is possible with today's tools.
- **Attach fluorescent marker materials to illuminate specific cancer cells, so that they are easier to locate and find for treatment,** whether drug delivery or surgery.

- **Deliver anti-cancer drugs for pinpoint targeted treatment of cancer cells, which should result in few drug side effects.** Currently, a cancer treatment like chemotherapy affects not only cancer cells but healthy cells as well, leading to serious and often debilitating side effects.

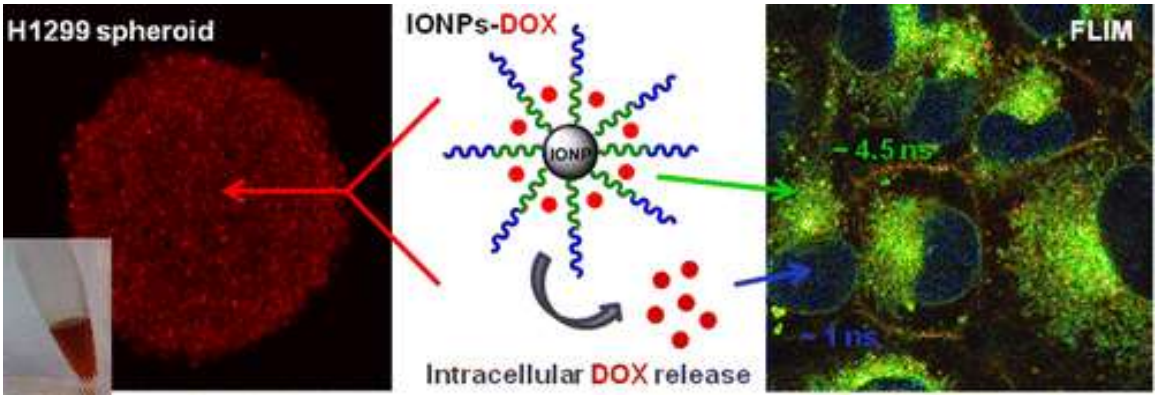
… (Source: University of Cincinnati)

☞ Integrated DNA Technologies Launches its First Cancer Panel

Integrated DNA Technologies (IDT) is enabling cancer research with its latest next generation sequencing (NGS) product, the xGen Acute Myeloid Leukemia Cancer Panel v1.0. Consisting of 11,743 xGen Lockdown Probes, this cancer panel targets more than 260 clinically relevant genes that were found to be mutated in a study of 200 patients with acute myeloid leukemia (AML), and published by The Cancer Genome Atlas consortium. The AML Cancer Panel is used for enriching the genome for regions of interest before performing NGS. It can, therefore, be used to study disease occurrence and progression, and help with the development of better targeted therapies. … (Source: CPhI)

☞ Using Fluorescence Lifetime Imaging Microscopy to Monitor Theranostic Nanoparticle Uptake and Intracellular Doxorubicin Release

Basuki J et Al. *ACS Nano*, Article ASAP DOI: 10.1021/nn404407g - Publication Date (Web): October 16, 2013



We describe the synthesis of iron oxide nanoparticles (IONPs) with excellent colloidal stability in both water and serum, imparted by carefully designed grafted polymer shells. The polymer shells were built with attached aldehyde functionality to enable the reversible attachment of doxorubicin (DOX) *via* imine bonds, providing a controlled release mechanism for DOX in acidic environments. The IONPs were shown to be readily taken up by cell lines (MCF-7 breast cancer cells and H1299 lung cancer cells), and intracellular release of DOX was proven using *in vitro* fluorescence lifetime imaging microscopy (FLIM) measurements. Using the fluorescence lifetime difference exhibited by native DOX (~1 ns) compared to conjugated DOX (~4.6 ns), the intracellular release of conjugated DOX was *in situ* monitored in H1299 and was estimated using phasor plot representation, showing a clear increase of native DOX with time. The results obtained from FLIM were corroborated using confocal microscopy, clearly showing DOX accumulation in the nuclei. The IONPs were also assessed as MRI negative contrast agents. We observed a significant change in the transverse relaxivity properties of the IONPs, going from 220 to 390 mM^{-1} s^{-1}, in the presence or absence of conjugated DOX. This dependence of MRI signal on IONP-DOX/water interactions may be exploited in future theranostic applications. The *in vitro* studies were then extended to monitor cell uptake of the DOX loaded IONPs (IONP@P(HBA)-*b*-P(OEGA) + DOX) into two 3D multicellular tumor spheroids (MCS) grown

from two independent cell lines (MCF-7 and H1299) using multiphoton excitation microscopy. … (Source: ACS)

☞ Cryo-EM Structure of a Fully Glycosylated Soluble Cleaved HIV-1 Envelope Trimer

Lyumkis D et Al. *Science DOI: 10.1126/science.1245627*

The HIV-1 envelope glycoprotein (Env) trimer contains the receptor binding sites and membrane fusion machinery that introduce the viral genome into the host cell. As the only target for broadly neutralizing antibodies (bnAbs), Env is a focus for rational vaccine design. We present a cryo-electron microscopy reconstruction and structural model of a cleaved, soluble SOSIP gp140 trimer in complex with a CD4 binding site (CD4bs) bnAb, PGV04, at 5.8 Å resolution. The structure reveals the spatial arrangement of Env components, including the V1/V2, V3, HR1 and HR2 domains, and shielding glycans. The structure also provides insights into trimer assembly, gp120-gp41 interactions, and the CD4bs epitope cluster for bnAbs, which covers a more extensive area and defines a more complex site of vulnerability than previously described. … (Source: ScienceJournals)

☞ The Major Brain Cholesterol Metabolite 24(S)-Hydroxycholesterol Is a Potent Allosteric Modulator of *N*-Methyl-d-Aspartate Receptors

Steven P. et Al. The Journal of Neuroscience, 30 October 2013, 33(44): 17290-17300; doi: 10.1523/JNEUROSCI.2619-13.2013

N-methyl-d-aspartate receptors (NMDARs) are glutamate-gated ion channels that are critical to the regulation of excitatory synaptic function in the CNS. NMDARs govern experience-dependent synaptic plasticity and have been implicated in the pathophysiology of various neuropsychiatric disorders including the cognitive deficits of schizophrenia and certain forms of autism. Certain neurosteroids modulate NMDARs experimentally but their low potency, poor selectivity, and very low brain concentrations make them poor candidates as endogenous ligands or therapeutic agents. Here we show that the major brain-derived cholesterol metabolite 24(S)-hydroxycholesterol (24(S)-HC) is a very potent, direct, and selective positive allosteric modulator of NMDARs with a mechanism that does not overlap that of other allosteric modulators. At submicromolar concentrations 24(S)-HC potentiates NMDAR-mediated EPSCs in rat hippocampal neurons but fails to affect AMPAR or $GABA_A$ receptors ($GABA_A$Rs)-mediated responses. Cholesterol itself and other naturally occurring oxysterols present in brain do not modulate NMDARs at concentrations ≤10 μm. In hippocampal slices, 24(S)-HC enhances the ability of subthreshold stimuli to induce long-term potentiation (LTP). 24(S)-HC also reverses hippocampal LTP deficits induced by the NMDAR channel blocker ketamine. Finally, we show that synthetic drug-like derivatives of 24(S)-HC, which potently enhance NMDAR-mediated EPSCs and LTP, restore behavioral and cognitive deficits in rodents treated with NMDAR channel blockers. Thus, 24(S)-HC may function as an endogenous modulator of NMDARs acting at a novel oxysterol modulatory site that also represents a target for therapeutic drug development. … (Source: TheJournalOfNeuroscience)

☞ Genetic basis of neurocognitive decline and reduced white-matter integrity in normal human brain aging

Glahn D. et Al. doi: 10.1073/pnas.1313735110 PNAS November 4, 2013

Identification of genes associated with brain aging should markedly improve our understanding of the biological processes that govern normal age-related decline. However, challenges to identifying genes that facilitate successful brain aging are considerable, including a lack of established phenotypes and difficulties in modeling the effects of aging per se, rather than genes that influence the underlying trait. In a large cohort of randomly selected pedigrees (*n* = 1,129 subjects), we documented profound aging effects from young adulthood to old age (18–83 y) on neurocognitive ability and diffusion-based white-matter measures. Despite significant phenotypic correlation between white-matter integrity and tests of processing speed, working memory, declarative memory, and intelligence, no evidence for pleiotropy between these classes of phenotypes was observed. Applying an advanced quantitative gene-by-environment interaction analysis where age is treated as an environmental factor, we demonstrate a heritable basis for neurocognitive deterioration as a function of age. Furthermore, by decomposing gene-by-aging (G × A) interactions, we infer that different genes influence some neurocognitive traits as a function of age, whereas other neurocognitive traits are influenced by the same genes, but to differential levels, from young adulthood to old age. In contrast, increasing white-matter incoherence with age appears to be nongenetic. These results clearly demonstrate that traits sensitive to the genetic influences on brain aging can be identified, a critical first step in delineating the biological mechanisms of successful aging. … (Source: PNAS)

☞ BI HCV drug faldaprevir shows promise

Boehringer Ingelheim has presented new data from a Phase III trial programme which shows that faldaprevir was highly effective in a broad range of patients with genotype-1 hepatitis C.

The study, the data from which were presented at the Liver Meeting in Washington DC, evaluated faldaprevir in combination with pegylated interferon and ribavirin in treatment-naive and experienced patients as well as in HIV co-infected participants.

Among the highlights of the data, in the STARTVerso 1 and 2 trials, 84% of treatment-naïve patients receiving faldaprevir were able to shorten the total time on treatment from 48 to 24 weeks and 83% of these patients achieved viral cure (SVR12). Interim results from STARTVerso 4 showed that 74% of patients with HCV/HIV co-infection had undetectable HCV four weeks after the conclusion of treatment. … (Source: PharmaTimes)

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